

REMARKS/ARGUMENTS

Claims 1-5, 7-11, 13-21, 23-25, 27-30, 39, 41, 44-53, and 62 are pending. Claims 1, 11, 15, 23-25, 27-30, 39, and 41 have been amended and claim 62 is new. Support for the amendments to claim 1 may be found at least in paragraphs [0020]-[0021] of the instant application, as published (i.e., Published Application No. US2007/0031339). Claims 11, 15, 23-25, 27-30, 39, and 41 have, for the most part, been amended so that those claims comport with the language in claim 1. Support for claim 62 may be found at least in claim 15. No new matter has been introduced by way of these amendments or the added claim. Claims 16, 28-30, and 44-53 stand withdrawn and claims 6, 12, 22, 26, 31-38, 40, 42, 43, and 54-61 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the withdrawn and/or cancelled claims in continuing applications.

I. *The Obviousness-Type Double Patenting Rejection Should At Least Be Held in Abeyance*

Claims 1-5, 7-11, 13-15, 17-21, 23-25, 27, and 39-43 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting (ODP) as being unpatentable over claims of co-pending Appl. Ser. No. 11/913,079. Applicants understand that this is a “provisional” double patenting rejection and that the Patent Office will continue to make this rejection so long as there are conflicting claims in more than one application, unless that “provisional” double patenting rejection is the only rejection remaining in at least one of the applications. *MPEP* § 804. Applicants also understand that if a “provisional” non-statutory ODP rejection is the only rejection remaining in the **earlier filed** of the two pending applications (i.e., the instant case), while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application (i.e., the instant application) to issue as a patent without a terminal disclaimer. *Id.*

Since no claims in either application have yet been held allowable, Applicants respectfully ask the Patent Office to at least hold this rejection in abeyance until the claims in the instant application have been agreed to be otherwise allowable. Once the instant claims have been deemed otherwise allowable, and the ODP rejection is the only remaining rejection in the instant case, the Patent Office is urged to withdraw the rejection and permit the instant application to issue.

II. *The Amended Claims Overcome the Rejection Under 35 U.S.C. § 103(a)*

Claims 1-5, 7-11, 13-15, 17-21, 23-25, 27, and 39-43 stand rejected under 35 U.S.C. § 130(a) over the teachings of Guillet (US2003/0177868) in view of Mao et al. (U.S. Patent No. 6,686,308) for the reasons set forth on pages 3-5 of the Office Action. In addition, claims 1, 7-10, 13-15, 20, 21, 23-25, 27, and 39-43 stand rejected under 35 U.S.C. § 130(a) over Rioux et al. (US2004/0101564) for the reasons set forth on pages 5 and 6 of the Office Action. Applicants respectfully submit that the amended claims overcome these rejections for at least the reasons set forth below.

Claim 1, as amended, is directed to a particle comprising a metallic core and a charged coating layer overlying the core. The coating layer comprises an acrylic acid polymer and has a density sufficient to passivate the core. The core comprises 20% by weight or greater of tungsten. The particle is of sufficient size to provide X-ray attenuating properties as an X-ray contrast agent. The particle is also of a size that is below a kidney threshold size.

Guillet discloses internally cross-linked, stable polymeric materials, in the form of substantially spherical particles, each particle consisting essentially of a single macromolecule. Guillet abstract. According to Guillet, his polymer particles are useful in imaging applications, such as in jet printing. *Id.* at ¶[0033]. Because of their ability to “scarcely affect the viscosity” of a solution or of a dispersion into which they are placed, Guillet states that his particles could also be useful in drug delivery applications. *Id.* at ¶[0006]. Finally, in one aspect, Guillet’s particles are used in the preparation of nanoparticles of metals, where the metal nanoparticles have diameters ranging from 0.1-10. *Id.* at ¶[0032]. Once the particles are made, the polymer content is **largely removed** by pyrolysis, leaving extremely small metal particles, that, in some instances, are “surrounded by a fine layer of residual polymer which has a stabilizing effect.” *Id.* at ¶¶ [0032]-[0033] (emphasis added). According to Guillet, such metal particles are useful in imaging such as inkjet printing and, because of their very high surface area, in catalysis. *Id.* at ¶[0033]. Although Guillet states that “palladium, platinum, titanium and molybdenum are examples of metals which can be prepared in nanoparticle form” according to his invention, for use in catalysis, he is

completely silent with regard to tungsten. *See* ¶[0032]. Likewise, Guillet is silent with regard to whether the metal particles he discloses would be suitable for administration to a human subject in a pharmaceutical composition such as the one claimed in instant claim 39. Indeed, the thrust of Guillet is either inkjet printing or catalysis, not pharmaceutical compositions.

Mao discloses a supported catalyst comprising catalyst metal nanoparticles having an average particle size of 3.0 nm or less. Mao abstract. Typical catalyst metals disclosed by Mao are selected from platinum, palladium, ruthenium, rhodium, iridium, osmium, molybdenum, tungsten, iron, nickel and tin. *Id.* Typical support particles are carbon. Mao, like Guillet, is silent with regard to whether his metal nanoparticles would be suitable for administration to a human subject in a pharmaceutical composition such as the one claimed in instant claim 39. Indeed, the thrust of Mao is catalysis, not pharmaceutical compositions.

The U.S. Supreme Court held that rigid and mandatory application of the “teaching-suggestion-motivation,” or TSM, test is incompatible with its precedents. *KSR Int’l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007). The Court did not, however, discard the TSM test completely; it noted that its precedents show that an invention “composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *Id.* The Court held that “it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements in the way the claimed new invention does.” *Id.* “To facilitate review, this analysis should be made explicit.” *Id.* The obviousness rationale addressed in *KSR* was premised on combining elements known in the prior art. *Id.* at 1738-39. A parallel analysis applies to a rejection premised on the obviousness of modifying Guillet thereby arriving at the presently claimed composition. In particular, the *KSR* Court noted that obviousness cannot be proven merely by showing that the elements of a claimed device were known in the prior art; it must be shown that those of ordinary skill in the art would have had some “apparent reason to combine the known elements in the fashion claimed.” *Id.* at 1741.

Applicants submit that there simply is no reason why those of ordinary skill in the art would combine the elements in two references that are in the field of catalysis to arrive at particles having X-ray attenuating properties, as do the claimed particles. Applicants would go as far as saying that these references, in fact, teach away from having a coated particle

because a metal particle used in catalysis requires that the metal be exposed, not coated. Guillet even goes as far as teaching the removal of the polymer coating from the metal nanoparticles he generates. Guillet at ¶ [0032] (“The polymer coating is largely removed by pyrolysis”). In sum, Applicants submit that the combined teachings of Guillet and Mao do not render the claimed invention obvious. Reconsideration and withdrawal of the rejection over Guillet in view of Mao are respectfully requested.

Applicants submit that the rejection of claims 1, 7-10, 13-15, 20, 21, 23-25, 27, and 39-43 over Rioux is overcome by the amendments to claim 1. Rioux teaches micron-size particles. In some embodiments, the particles have a mean diameter of from about ten microns to about 3,000 microns. Rioux at ¶¶ [0005]-[0007] and [0008]-[0013]. Rioux does not disclose or otherwise contemplate particles that are **both** of sufficient size to provide X-ray attenuating properties as an X-ray contrast agent **and** are of a size that is below a kidney threshold size. Accordingly, Rioux does not render the claimed invention obvious. Reconsideration and withdrawal of the rejection over Rioux are respectfully requested.

Applicant respectfully asserts that the claims submitted herewith fulfill the requirements of a patentable invention. Applicant also respectfully asks that all rejections and objections be withdrawn and that the pending claims be allowed.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

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